

## REMARKS

Reconsideration of this application, as amended, is respectfully requested. Claims 1 and 19 have been amended. Claim 35 has been cancelled. New claims 36-39 have been introduced. With this amendment, claims 1, 2, 4-19, 21-27, 32, 33 and 36-39 are pending in this application. These amendments are made without prejudice or disclaimer and do not include any new matter. Applicants reserve the right to prosecute any cancelled or otherwise unclaimed subject matter in this or another application. Consideration and entry of this amendment is respectfully requested.

## AMENDMENTS

Claim 1 has been amended such that the tumor antigen is administered “in a first form directly into at least one lymph node and subsequently administering the tumor antigen in a second form different from the first form directly into the at least one lymph node.” This amendment is fully supported by the originally-filed specification. For instance, at p. 30, lines 17-18, the specification states “[t]he same lymph node was injected on each occasion”. New claims 36-39 find support in the originally filed application at, for example, p. 9, lines 1-12 and Example 1. Thus, these amendments do not add any new matter.

## REJECTIONS UNDER 35 U.S.C. 103(a)

### **A. Claims 1, 2, 4-19, 21-27 and 32-35**

Claims 1-2, 4-17, and 32-35 stand rejected under 35 U.S.C. 103(a) over Hurpin, et al. (Vaccine, 16(2/3): 208-215 (1998)) in view of Hodge (Vaccine, 15(6/7): 759-768 (1997)), Rice (U.S. Pat. No. 6,127,116 (1997)), and Lehner, et al. (J. Inf. Dis. 179 (Suppl. 3): S489-S492 (1999)). Claim 34 has been previously cancelled; the rejection is therefore moot as to claim 34. Applicants respectfully traverse the remaining rejections as indicated below.

In the Office Action (pp. 2-3), it is alleged that Applicants’ previous argument related to Hurpin are incorrect “as both the spleen and lymph nodes serve similar functions” and, therefore, “the skilled artisan would have expected that delivery of vaccine to a lymphatic tissue, whether spleen or lymph node, would generate an immune

response...increased over subcutaneous delivery." Applicants respectfully disagree as the tissues are understood by those of skill in the art to be very different. Rice is alleged to teach the lymph node as the preferred route of administration and Lehner is alleged to "provide[] clear evidence that targeted delivery of antigen in the vicinity of lymph node[s] has a substantial effect in enhancing immune responses" at p. 4 of the Office Action. Applicants respectfully disagree, and believe that Rice does anything other than mention lymph node administration as a possible route of administration. Applicants also believe that Lehner merely demonstrates a subcutaneous method of administration. However, in order to expedite prosecution of this application, Applicants have amended claim 1 as described below.

Previously pending claim 35 was directed to administration of the first and second forms of the antigen are administered to the same lymph node. Claim 1 has been amended to incorporate this feature. The Office Action does not explain how any of the cited references would have motivated the skilled artisan to administer both forms of antigen to the same lymph node. Applicants respectfully maintain that, in fact, such an explanation could not be made because none of the cited references make any such suggestion. Hurpin could not have done so as the reference does not describe or suggest administration of antigen to any lymph node, but only the spleen. Hodge merely demonstrates administration of two different viruses by tail scarification in mice (e.g., a general disclosure of prime-boost). Rice does not suggest direct administration of antigen to a particular lymph node but simply suggests the lymphatic system as a possible route of immunization. And there is nothing in Lehner's description of a subcutaneous, indirect "targeted lymph node administration" (TILN) (e.g., as described by citation 8 of Lehner (Lehner, et al. J. Immunol. 153: 1858-1868 (1994))) that would suggest to one of skill in the art that the different forms of antigen should be directly administered to the same lymph node, as instantly claimed. As such, Applicants respectfully maintain that the cited combination of references cannot support a proper *prima facie* case of obviousness against the instantly pending claims. It is accordingly requested, therefore, that these rejections be withdrawn.

**B. Claims 18-19**

Claims 18 and 19 stand rejected under 35 U.S.C. 103(a) over Hurpin in view of Hodge, Rice, and Lehner, as applied in part A above and further in view of Zaremba, et al. (Cancer Res. 57: 4570-4577 (1997)) and Salgaller, et al. (Cancer Res. 56: 4749-4757 (1996)). Applicants respectfully traverse these rejections as indicated below.

Applicants have discussed the deficiencies of the rejection based on the combination of the Hurpin, Hodge, Rice and Lehner references above. As described therein, Applicants do not believe that the alleged combination of references support a proper *prima facie* case of obviousness. And Applicants do not believe Zaremba's disclosure of the peptide YLSGADLNL and / or Salgaller's disclosure of the peptide YLEPGPVTM would have motivated one of ordinary skill in the art to administer two forms of antigen to the same lymph node, as instantly claimed. As such, Applicants respectfully maintain that the instantly claimed methods are not obvious in view of this combination of references. Accordingly, it is respectfully requested that these rejections be withdrawn.

**C. Claims 21-27**

Claims 21-27 stand rejected under 35 U.S.C. 103(a) over Hurpin in view of Hodge, Rice, and Lehner as applied as applied in part A above and further in view of Barnett (Vaccine, 15(8): 869-873 (1997)). Applicants respectfully traverse these rejections as indicated below.

Applicants have discussed the deficiencies of the rejection based on the combination of the Hurpin, Hodge, Rice and Lehner references above. As described therein, Applicants do not believe that the references can be combined to render the pending claims obvious. And Applicants do not believe Barnett's alleged disclosure of a prime/boost vaccination strategy using nucleic acid and protein forms of antigen would have motivated one of ordinary skill in the art to administer two forms of antigen to the same lymph node, as instantly claimed. As such, Applicants respectfully maintain that the instantly claimed methods are not obvious in view of this combination of references. Accordingly, it is respectfully requested that these rejections be withdrawn.

### CONCLUSIONS

Consideration and entry of this response is respectfully requested. Applicants believe the claims are now in condition for allowance, and respectfully request that a Notice of Allowance be issued as soon as possible. The Examiner is encouraged to contact the undersigned if it is believed doing so would assist in the examination of this application.

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